THE CLAIMS

What is claimed is:

1. A polypeptide comprising a single-domain of the variable region of the heavy chain of an antibody molecule, which is soluble and stable and capable of binding a specific antigen of interest, said polypeptide comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, said VH/VL interface comprising at least one charged residue.

2. The polypeptide of claim 1 wherein the polypeptide is substantially monomeric.

3. The polypeptide of claim 1, wherein the polypeptide is encoded by a polynucleotide isolated from a phage clone selected from a phage-display library comprising a plurality of recombinant phage, each of said recombinant phages having an expression vector encoding a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, having a unique VH/VL interface comprising at least one charged residue and a randomized CDR3.

4. The polypeptide of claim 3 wherein the selected clone is produced in E. coli as insoluble inclusion bodies and the isolated polypeptide is subsequently refolded in-vitro and purified.

5. The polypeptide claim 3 wherein the scaffold element representing the VH/VL interface comprises the sequence Lysine-44, Leucine-45, and Tryptophan-47.

6. The polypeptide of claim 1 wherein the specific antigen of interest is an immunoglobulin molecule.

7. The polypeptide of claim 3 wherein the CDR3 sequence between residues 95 and 100C comprises the consensus sequence: Gly-X-Ser-Pro-Gln, wherein X represents any amino acid.

8. The polypeptide of claim 3 wherein the CDR3 sequence between residues 95 and 100C is selected from the sequences: Gln-Ser-Gly-Gln-Ser-Pro-Gln-Ser-Ile, and Asn-Gly-Lys-Ser-Pro-Gln-Ala-Ala-Trp.

9. The polypeptide of claim 1 wherein the specific antigen of interest is tumor necrosis factor.

10. The polypeptide of claim 9 wherein the CDR3 sequence between residues 95 and 100C comprises the sequence: Phe-Pro-Thr-Gly-Asp-Leu-Ala-Glu-Lys.

11. The polypeptide of claim 1 wherein the specific antigen of interest is Streptavidin.

12. The polypeptide of claim 11 wherein the CDR3 sequence between residues 95 and 100C is selected from the sequences: His-Ala-Gln-Arg-Arg-Pro-Trp-Ile-Arg, and Glu-Asp-Pro-His-Pro-Gln-Arg-Gly-Tyr.

13. A peptide capable of binding a specific antigen of interest, said peptide being derived from the randomized sequence of the CDR3 region of a polypeptide comprising a single-domain of the variable region of the heavy chain of an antibody molecule, which is soluble and stable and capable of binding said specific antigen of interest, said polypeptide comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, said VH/VL interface comprising at least one charged residue.

14. The peptide of claim 13 wherein the polypeptide is encoded by a polynucleotide isolated from a phage clone selected from a phage-display library comprising a plurality of recombinant phage, each of said recombinant phages having an expression

vector encoding a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal antibody without induced mutations or modifications in the original VH/VL interface framework residues, having a unique VH/VL interface comprising at least one charged residue and a randomized CDR3.

15. The peptide of claim 13 wherein the peptide comprises 4-20 amino acids.

16. The peptide of claim 13 wherein the peptide comprises 7-15 amino acids.

17. The peptide of claim 13 wherein the specific antigen of interest is an immunoglobulin molecule.

18. The peptide of claim 13 wherein the specific antigen of interest is tumor necrosis factor.

19. A pharmaceutical composition comprising as an active ingredient the polypeptide of claim 1, and a physiologically acceptable diluent or carrier.

20. A pharmaceutical composition comprising as an active ingredient the peptide of claim 13, and a physiologically acceptable diluent or carrier.

21. A phage-display library comprising a plurality of recombinant phage, each of said recombinant phage having an expression vector encoding a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal antibody without any mutations or modifications in the original interface framework residues, having a unique VH/VL interface comprising at least one charged residue, and a randomized CDR3.

22. The phage display library of claim 21 wherein the single-domain variable region of the heavy chain is substantially monomeric.

23. The phage display library of claim 21 wherein the scaffold element representing the VH/VL interface comprises the sequence Lysine-44, Leucine-45, and Tryptophan-47.

24. An isolated phage clone which binds selectively to a specific antigen of interest, said clone being selected from a phage-display library comprising a plurality of recombinant phage, each of said recombinant phage having an expression vector encoding a single-domain of the variable region of the heavy chain of an antibody molecule comprising a natural framework scaffold of a mammalian monoclonal antibody without any mutations or modifications in the original interface framework residues, having a unique VH/VL interface and a randomized CDR3.

25. The isolated phage clone of claim 24 wherein the phage display library comprises a scaffold element representing the VH/VL interface comprising the sequence Lysine-44, Leucine-45, and Tryptophan-47.

26. The isolated phage clone of claim 24 encoding a polypeptide wherein the specific antigen of interest is an immunoglobulin molecule.

27. The isolated phage clone of claim 24 encoding a polypeptide wherein the specific antigen of interest is tumor necrosis factor.

28. A method of treatment of a disease comprising administering to a patient in need thereof a pharmaceutical composition comprising as an active ingredient a therapeutically effective amount of the polypeptide of claim 1.

29. A method of diagnosis of a disease comprising administering to a patient in need thereof a pharmaceutical composition comprising as an active ingredient the polypeptide of claim 1 in an amount which is effective to diagnose the disease.

30. A method of treatment of a disease comprising administering to a patient in need thereof a pharmaceutical composition comprising as an active ingredient a therapeutically effective amount of the polypeptide of claim 13.

31. A method of diagnosis of a disease comprising administering to a patient in need thereof a pharmaceutical composition comprising as an active ingredient the polypeptide of claim 13 in an amount which is effective to diagnose the disease.

32. A method of treatment of a disease comprising administering to a patient in need thereof a pharmaceutical composition comprising as an active ingredient a therapeutically effective amount of the polypeptide of claim 9.

33. A method of diagnosis of a disease comprising administering to a patient in need thereof a pharmaceutical composition comprising as an active ingredient the polypeptide of claim 9 in an amount which is effective to diagnose the disease.